



KCNQ1 gene

potassium voltage-gated channel subfamily Q member 1

Normal Function

The *KCNQ1* gene belongs to a large family of genes that provide instructions for making potassium channels. These channels, which transport positively charged atoms (ions) of potassium out of cells, play key roles in a cell's ability to generate and transmit electrical signals.

The specific function of a potassium channel depends on its protein components and its location in the body. Channels made with the KCNQ1 protein are active in the inner ear and in heart (cardiac) muscle. In the inner ear, these channels help maintain the proper ion balance needed for normal hearing. In the heart, the channels are involved in recharging the cardiac muscle after each heartbeat to maintain a regular rhythm. The KCNQ1 protein is also produced in the kidney, lung, stomach, and intestine, where it is involved in transporting molecules across cell membranes.

The KCNQ1 protein interacts with proteins in the KCNE family (such as the KCNE1 protein) to form functional potassium channels. Four alpha subunits made from the KCNQ1 protein form the structure of each channel. One beta subunit, made from a KCNE protein, attaches (binds) to the channel and regulates its activity.

Health Conditions Related to Genetic Changes

familial atrial fibrillation

Changes in the *KCNQ1* gene are an uncommon cause of familial atrial fibrillation, a disruption of the heart's normal rhythm (arrhythmia) characterized by uncoordinated electrical activity in the heart's upper chambers (the atria). Several mutations have been found to cause the condition; these genetic changes alter single protein building blocks (amino acids) in the KCNQ1 protein. In cardiac muscle cells, the mutations appear to increase the flow of potassium ions through the channel formed with the KCNQ1 protein. The enhanced ion transport can disrupt the heart's normal rhythm, resulting in atrial fibrillation.

Jervell and Lange-Nielsen syndrome

At least 16 *KCNQ1* gene mutations have been found to cause Jervell and Lange-Nielsen syndrome, a condition that causes arrhythmia and profound hearing loss from birth. These mutations are typically present in both copies of the *KCNQ1* gene in each cell. Most of these changes lead to the production of an abnormally short, nonfunctional version of the KCNQ1 protein that cannot be used to build potassium

channels. Other mutations change a small number of amino acids in this protein, which alters the normal structure and function of the channels. An inability of these channels to properly transport potassium ions in the inner ear and cardiac muscle leads to the hearing loss and arrhythmia characteristic of Jervell and Lange-Nielsen syndrome.

Romano-Ward syndrome

Changes in the *KCNQ1* gene are thought to be the most common cause of Romano-Ward syndrome, often called long QT syndrome. This condition causes the heart (cardiac) muscle to take longer than usual to recharge between beats, which can lead to arrhythmia.

More than 500 *KCNQ1* gene mutations that cause Romano-Ward syndrome have been identified. Unlike the mutations associated with Jervell and Lange-Nielsen syndrome, the mutations that cause Romano-Ward syndrome are typically present in only one copy of the *KCNQ1* gene in each cell. Most of these mutations change single amino acids in the *KCNQ1* protein or insert or delete a small number of amino acids. These changes allow the protein to form channels but reduce the channels' ability to transport potassium ions out of cardiac muscle cells. The reduced ion transport alters the transmission of electrical signals in the heart, increasing the risk of an irregular heartbeat that can cause fainting (syncope) or sudden death.

short QT syndrome

At least one mutation in the *KCNQ1* gene can cause a heart condition called short QT syndrome. In people with this condition, the cardiac muscle takes less time than usual to recharge between beats. This change increases the risk of an abnormal heart rhythm that can cause syncope or sudden death.

The *KCNQ1* gene mutation associated with short QT syndrome replaces the amino acid valine with the amino acid leucine at protein position 307 (written as Val307Leu or V307L). The mutation alters the function of ion channels made with the *KCNQ1* protein, increasing the channels' activity. As a result, more potassium ions flow out of cardiac muscle cells at a critical time during the heartbeat, which can lead to an irregular heart rhythm.

other disorders

Mutations in the *KCNQ1* gene have been associated with several other conditions related to heart rhythm abnormalities, including sudden infant death syndrome (SIDS) and acquired long QT syndrome.

SIDS is a major cause of death in babies younger than one year. It is characterized by sudden and unexplained death, usually during sleep. Although the cause of SIDS is often unknown, researchers have identified mutations in the *KCNQ1* gene in a few

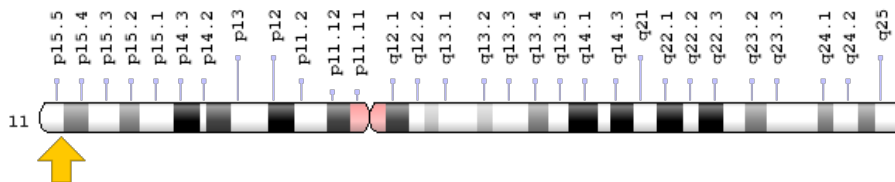
cases of this condition. Other genetic and environmental factors, many of which have not been identified, also play a part in determining the risk of SIDS.

Certain drugs, including medications used to treat arrhythmias, infections, seizures, and psychotic disorders, can lead to an abnormal heart rhythm in some people. This drug-induced heart condition, which is known as acquired long QT syndrome, increases the risk of cardiac arrest and sudden death. A small percentage of cases of acquired long QT syndrome occur in people who have an underlying variation in the *KCNQ1* gene.

Chromosomal Location

Cytogenetic Location: 11p15.5-p15.4, which is the short (p) arm of chromosome 11 between positions 15.5 and 15.4

Molecular Location: base pairs 2,444,991 to 2,849,110 on chromosome 11 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ATFB1
- IKs producing slow voltage-gated potassium channel alpha subunit KvLQT1
- JLNS1
- KCNA8
- KCNA9
- KCNQ1_HUMAN
- KQT-like 1
- Kv1.9
- Kv7.1
- KVLQT1
- LQT1

- potassium channel, voltage gated KQT-like subfamily Q, member 1
- potassium voltage-gated channel, KQT-like subfamily, member 1

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Specific Channels Can Rapidly Transport Ions Across Membranes
<https://www.ncbi.nlm.nih.gov/books/NBK22509/>
- Neuromuscular Disease Center, Washington University: KCNQ family of potassium channels
<http://neuromuscular.wustl.edu/mother/chan.html#kcnqfam>

GeneReviews

- Jervell and Lange-Nielsen Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1405>
- Long QT Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1129>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28KCNQ1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D>

OMIM

- POTASSIUM CHANNEL, VOLTAGE-GATED, KQT-LIKE SUBFAMILY, MEMBER 1
<http://omim.org/entry/607542>
- SUDDEN INFANT DEATH SYNDROME
<http://omim.org/entry/272120>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_KCNQ1.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=KCNQ1%5Bgene%5D>
- HGNC Gene Family: Potassium voltage-gated channels
<http://www.genenames.org/cgi-bin/genefamilies/set/274>

- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=6294
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/3784>
- UniProt
<http://www.uniprot.org/uniprot/P51787>

Sources for This Summary

- Arnestad M, Crotti L, Rognum TO, Insolia R, Pedrazzini M, Ferrandi C, Vege A, Wang DW, Rhodes TE, George AL Jr, Schwartz PJ. Prevalence of long-QT syndrome gene variants in sudden infant death syndrome. *Circulation*. 2007 Jan 23;115(3):361-7. Epub 2007 Jan 8.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17210839>
- Bellocq C, van Ginneken AC, Bezzina CR, Alders M, Escande D, Mannens MM, Baró I, Wilde AA. Mutation in the KCNQ1 gene leading to the short QT-interval syndrome. *Circulation*. 2004 May 25;109(20):2394-7.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15159330>
- Chan PJ, Osteen JD, Xiong D, Bohnen MS, Doshi D, Sampson KJ, Marx SO, Karlin A, Kass RS. Characterization of KCNQ1 atrial fibrillation mutations reveals distinct dependence on KCNE1. *J Gen Physiol*. 2012 Feb;139(2):135-44. doi: 10.1085/jgp.201110672. Epub 2012 Jan 16.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/22250012>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3269792/>
- Ellinor PT, Moore RK, Patton KK, Ruskin JN, Pollak MR, Macrae CA. Mutations in the long QT gene, KCNQ1, are an uncommon cause of atrial fibrillation. *Heart*. 2004 Dec;90(12):1487-8.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15547041>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1768565/>
- GeneReview: Jervell and Lange-Nielsen Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1405>
- GeneReview: Long QT Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1129>
- Herbert E, Trusz-Gluza M, Moric E, Smilowska-Dzielicka E, Mazurek U, Wilczok T. KCNQ1 gene mutations and the respective genotype-phenotype correlations in the long QT syndrome. *Med Sci Monit*. 2002 Oct;8(10):RA240-8. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12388934>
- Hong K, Piper DR, Diaz-Valdecantos A, Brugada J, Oliva A, Burashnikov E, Santos-de-Soto J, Grueso-Montero J, Diaz-Enfante E, Brugada P, Sachse F, Sanguinetti MC, Brugada R. De novo KCNQ1 mutation responsible for atrial fibrillation and short QT syndrome in utero. *Cardiovasc Res*. 2005 Dec 1;68(3):433-40. Epub 2005 Aug 18.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16109388>
- Huang L, Bitner-Glindzicz M, Tranebjaerg L, Tinker A. A spectrum of functional effects for disease causing mutations in the Jervell and Lange-Nielsen syndrome. *Cardiovasc Res*. 2001 Sep;51(4):670-80.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11530100>

- Jespersen T, Grunnet M, Olesen SP. The KCNQ1 potassium channel: from gene to physiological function. *Physiology (Bethesda)*. 2005 Dec;20:408-16. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16287990>
- Melman YF, Um SY, Krumerman A, Kagan A, McDonald TV. KCNE1 binds to the KCNQ1 pore to regulate potassium channel activity. *Neuron*. 2004 Jun 24;42(6):927-37.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15207237>
- Park KH, Piron J, Dahimene S, Mérot J, Baró I, Escande D, Loussouarn G. Impaired KCNQ1-KCNE1 and phosphatidylinositol-4,5-bisphosphate interaction underlies the long QT syndrome. *Circ Res*. 2005 Apr 15;96(7):730-9. Epub 2005 Mar 3.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15746441>
- Paulussen AD, Gilissen RA, Armstrong M, Doevendans PA, Verhasselt P, Smeets HJ, Schulze-Bahr E, Haverkamp W, Breithardt G, Cohen N, Aerssens J. Genetic variations of KCNQ1, KCNH2, SCN5A, KCNE1, and KCNE2 in drug-induced long QT syndrome patients. *J Mol Med (Berl)*. 2004 Mar;82(3):182-8. Epub 2004 Feb 4.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14760488>
- Tristani-Firouzi M, Sanguinetti MC. Structural determinants and biophysical properties of HERG and KCNQ1 channel gating. *J Mol Cell Cardiol*. 2003 Jan;35(1):27-35. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12623297>
- Wang Z, Li H, Moss AJ, Robinson J, Zareba W, Knilans T, Bowles NE, Towbin JA. Compound heterozygous mutations in KvLQT1 cause Jervell and Lange-Nielsen syndrome. *Mol Genet Metab*. 2002 Apr;75(4):308-16.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12051962>

Reprinted from Genetics Home Reference:
<https://ghr.nlm.nih.gov/gene/KCNQ1>

Reviewed: June 2013

Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services